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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/709,691	05/24/2004	Itzhak Bentwich	050992.0400.01USCP	3690
37808	7590	09/19/2007		
ROSETTA-GENOMICS c/o PSWS 700 W. 47TH STREET SUITE 1000 KANSAS CITY, MO 64112			EXAMINER WOLLENBERGER, LOUIS V	
			ART UNIT 1635	PAPER NUMBER
			MAIL DATE 09/19/2007	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/709,691	<b>Applicant(s)</b> BENTWICH ET AL.	
	<b>Examiner</b> Louis V. Wollenberger	<b>Art Unit</b> 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 29 June 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 23-38 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 23-38 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 24 May 2004 and 29 June 2007 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |                                                                                                            |                                                                                         |
|------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____                                                |

## **DETAILED ACTION**

### ***Election/Restrictions/ Status of Application/Amendment/Claims***

Applicant's election without traverse of Group I, drawn to an isolated nucleic acid, in the reply filed on 6/29/07, is acknowledged. Also acknowledged is Applicant's election without traverse of SEQ ID NO:348. Applicant states SEQ ID NO:348 corresponds to human target gene SERPINH1.

Applicant's cancellation of claims 1-22 renders moot the Restriction mailed 3/19/07.

Applicant presents new claims 23-38 by way of amendment, stating new claims 23-38 read on Group I, set forth in the Restriction mailed 3/19/07.

With entry of the amendment filed on 6/29/07, claims 23-38 are pending and examined herein.

### ***Sequence Compliance***

The objection to the disclosure for failing to provide SEQ ID NO: identifiers is withdrawn in view of applicant's amendments to the specification and drawings. Applicant also states the amendments bring the specification and drawings into compliance with 37 CFR §1.821-1.825. See Applicant's Remarks submitted 6/29/07, page 13.

### ***Claim Rejections - 35 USC § 112, second paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Art Unit: 1635

Claims 23-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 23 is drawn in part to an RNA equivalent of a nucleic acid 19-140 nucleotides in length comprising SEQ ID NO:348. However, the Office's records show that SEQ ID NO:348 is an RNA. Thus, it is unclear what is meant by the limitation an "RNA equivalent" of an RNA. The structures specifically included and/excluded by this limitation are unclear. Accordingly, one of skill in the art would not be apprised of the metes and bounds of the claim as a whole.

Dependent Claims 24-38 are rejected therefor.

Correction is required.

***Claim Rejections - 35 USC § 101 and 112, First Paragraph***

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 23-38 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility, a credible asserted utility, or a well established utility.

Art Unit: 1635

The claims are drawn to an isolated nucleic acid sequence consisting of 19 to 140 nucleotides comprising (a) SEQ ID NO: 348; b) an RNA equivalent of (a); c) a sequence at least 63.7% identical to (a) or (b); or d) the complement of any one of (a)-(c).

In one embodiment, claims 24 and 26, the sequence comprises or consists of SEQ ID NO:4,233,864, a 91-nucleotide RNA.

Also claimed are vectors thereof.

Thus, the claims are extremely broad, embracing not only the sequences themselves, but subsequences thereof, with as little as 63.7% identity, as well as any complement of such sequences.

At the outset, it is noted that the instant application is extremely large, comprising a 162-page specification, and at least 15 different mega tables, disclosing several million different nucleic acid sequences, said to be precursor and processed miRNAs, with homologies to a variety of different targets, and having a wide variety of asserted utilities based on that homology.

Written description and enabling support describing and teaching methods for using instant SEQ ID NO:348 and 4,233,864 for a substantial utility is not readily found therein.

Applicant states in the Remarks filed 6/29/07 that SEQ ID NO:348 corresponds to human target gene SERPINH1, but does not indicate where such support may be found in the instant application as originally filed.

The specification teaches that Micro RNAs (miRNAs), are short ~22nt non-coding regulatory RNA oligonucleotides, found in a wide range of species, believed to function as specific gene translation repressors, sometimes involved in cell-differentiation.

Art Unit: 1635

The specification teaches a bioinformatic method for detecting putative miRNA-like precursor sequences in the genome of an organism. Further bioinformatics processing is then used to predict the single stranded miRNAs likely produced from such sequences. Finally, the sequences of the predicted miRNAs are compared to sequences of known genes to identify potential targets and possible biological functions of the miRNAs.

While the specification teaches miRNA prediction, support is not readily found showing that the claimed miRNAs are actually produced in any cell or organism, or even if produced artificially, would lead to any biological effect of any immediate, real world value. No biologically relevant data, nor any intrinsic or extrinsic evidence is found in the instant application confirming any of the asserted utilities.

In the instant case the only utility readily identified has to do with that set forth in the Remarks filed 7/2/07, wherein Applicant asserts a relationship to SERPINH1.

A review of the pertinent literature indicates SERPINH1 is also known as homo sapiens serpin peptidase inhibitor, clade H, heat shock protein 47 (HSP47), member 1, and collagen binding protein 1.

The prior art (Sunamoto et al., Lab Invest., 1998 78:967-72, for example) teaches a possible correlation between HSP47 and fibrotic disease such as glomerulonephritis. Heat shock protein 47 (HSP47) is a collagen-specific molecular chaperone that has been reported to play a pivotal role in secretion of procollagen molecules (Hagiwara et al., J Gene Med. 2003 Sep;5(9):784-94). The expression of HSP47 is said to increase in parallel with the expression of collagens during the progression of various fibrosis models. However, Sunamoto et al. state it remains unclear whether an inhibition of HSP47 overexpression would suppress collagen

Art Unit: 1635

accumulation and thus reduce the progression of fibrotic diseases. While inhibition of HSP47 has been shown to suppress the production of collagen and attenuate the histologic manifestations of the disease in a model organism, it is unclear how these results may be extrapolated to the entire set of RNA sequences now claimed. It is not clear for example whether any of the sequences now claimed are capable of inhibiting HSP47 expression, and more importantly, whether any of the sequences now claimed would lead to any such treatment effect in any animal. Neither the instant application nor the prior art teaches one of skill how to use the multitude of RNA sequences now claimed, including complements and homologous sequences alike, to treat any fibrotic or other HSP47-related disease in any animal or human subject.

Indeed, the asserted utility and target gene of this and thousands of other miRNA-like sequences appears to be based purely on bioinformatic methods for predicting RNA folding and potential gene targets.

Post-filing art indicates that while prediction software and bioinformatics methods significantly narrow the field of possible sequences, they do not substitute for or render unnecessary the need for biological validation.

Krutzfeldt et al. (2006) *Nature Genetics* 38:514-519 state that, in general, the basis for these types of prediction programs is the degree of sequence complementarity between a miRNA and a target UTR, including the presence of a consecutive string of base pairs at the 5' end of the miRNA known as a 'seed' or 'nucleus', and the cross-species conservation of this binding site. On average, 200 genes are predicted to be regulated by a single miRNA. The authors further state that reviewing the data provided by these algorithms determining candidate targets uncovers the entire gamut of gene categories, such as transcription factors, protein kinases,

Art Unit: 1635

vesicular trafficking molecules and membrane receptors, suggesting that there is no apparent bias towards one particular function.

Bentwich (2005) *FEBS Lett.* 5904-5910 teaches that biological validation is necessary to raise the specificity and sensitivity of microRNA prediction algorithms, implying that predictions based on such algorithms need validation and that prediction does not guarantee that such a sequence exists or has the function assigned to it by the software.

Accordingly, while the ability to predict hairpin-like structures and potential gene targets from genomic sequence information appears to be within the state of the art, Krutzfeldt et al. and Bentwich teach that validating the true biological function of any predicted miRNA sequence requires analyzing miRNA expression patterns, as well as testing the effects of miRNA overexpression and underexpression under different conditions in living cells *in vitro* and *in vivo*. Thus, while these methods, too, are within the level of skill in the art, Applicant has presented no evidence that any of these validation techniques have, in fact, been carried out with regard to the instantly claimed sequences. As a result, one of skill would be left to de novo screening testing to identify such function, with no assurance that any practical or beneficial function would ever be identified.

Even more, Applicant seeks to claim not only the specified sequence, 348 and 4,233,864, but RNA equivalents, complements, and all sequences at least 63.7% identical to SEQ ID NO:348 and equivalents thereto. No evidence is remotely evident suggesting a substantial utility for all these sequences. For example, there is no evidence to suggest any sequence of 19-140 nts in length, 63.7% identical to SEQ ID NO:348 could be used to inhibit SERPINH1 in cells *in vivo* or produce any immediately available effect of real world value. The claims are extremely broad,



Art Unit: 1635

encompassing an enormous number of different sequences that could produce any number of different biological effects.

While the asserted utility, stated in the Remarks filed 6/29/07, may be credible and specific, it is not substantial. The specification does not establish a nexus between any particular disease state, condition, or biological process and the target gene, nor does the specification provide any evidence that the multitude of sequences now claimed would achieve any practical effect related to a disease, condition, or process that would enable one of skill to use the claimed sequences to achieve a beneficial effect.

While the oligonucleotides of the present invention may be useful for research purposes, in order to further understand the connection between the novel oligonucleotides of the present invention and disease, as either a diagnostic or a preventative, and for monitoring disease progress, these utilities are not specific, since the same can be done with any antisense polynucleotide. And because the specification does not disclose any specific function for the large number of nucleic acids now claimed, aside from indicating that it may be expressed in certain cells or present in certain genomes, it is unclear how or why one of skill in the art would use the information obtained by measuring or expressing sequences identical to or RNA equivalents of SEQ ID NO:348 for any particular purpose aside from general research. Further, since Applicant does not identify whether abnormal SEQ ID NO:348 or target gene expression is related to any disease or condition, or whether abnormal SEQ ID NO:348 or target gene function (e.g., a polymorphism) predisposes anyone to any disease or condition—the only recognizable utility of diagnostic probes is as tools for scientific research—and with no indication that anything useful will be discovered. Therefore, the asserted utility is not substantial since the

Art Unit: 1635

application provides no teaching regarding how to use the probes or expression data for any practical purpose beyond the art-recognized methods of gene expression analysis.

Accordingly, the instantly claimed nucleic acids are simply research intermediates that may be used to conduct further experimentation. The nucleic acids would provide no immediate, real-world information about the overall structure or function of the underlying gene, nor is there any guidance or evidence that the instant nucleic acids, much less the recited RNA equivalents thereof, have any specific biological function. No evidence or information is found either in the specification or the prior art linking SEQ ID NO:348 or any of its subsequences with the modulation of any gene or inhibition of any condition.

In fact, no evidence is found suggesting or stating that SEQ ID NO:348 has been made, isolated, cloned, detected, expressed, or even analyzed in a living cell *in vitro* or *in vivo*. In summary, no biological or biochemical function has been assigned to SEQ ID NO: 348 or 4,233,864, apart from the general assertions that it, like the thousands of other sequences described in the sequence listing, may correspond to an miRNA precursor and have some direct or indirect relation to gene expression and disease.

Thus, the proposed utilities of the instantly claimed nucleic acids as a therapeutic target or agent, or material resource for preparing diagnostic probes, inhibitory agents, vectors, and host cells, are simply starting points for further research and investigation into potential practical uses of the claimed polynucleotides.

Brenner v. Manson, 148 U.S.P.Q. 689 (U.S. 1966)

The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point—where specific benefit exists in currently

Art Unit: 1635

available form—there is insufficient justification for permitting an applicant to engross what may prove to be a broad field.

...a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.

Thus, the specification does not teach a specific and substantial utility for SEQ ID NO:348 or 4,233,864, much less any of the RNA equivalents or complements thereof. No target gene has been conclusively identified nor has any evidence been presented linking the claimed nucleic acids with any target gene, disease, or condition, biological function or disorder. A substantial nexus has not been established.

\*\*\*

Claims 23-38 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial, and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Art Unit: 1635

Claims 23, 25, and 27-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Random Primer 24, sold by New England Biolabs (see page 121 of the 1998/99 New England Biolabs Catalog) (New England Biolabs 1998/99 Catalog, cover page, page 121 and 284).

The limitation “the complement of any one of (a)-(c)” is interpreted to include both RNA and DNA nucleic acids, since RNA may be complementary to DNA and vice versa. Therefore, the claims embrace both DNA and RNA nucleic acids.

Random Primer 24 contains every possible 24-nucleotide sequence. The following calculations rely on facts provided on page 284 of the catalog, specifically the mass of 1.0 A<sub>260</sub> unit of single-stranded DNA and the molecular weight of single-stranded DNA per nucleotide (i.e. half the weight of a double-stranded DNA per basepair):

Random 24-mer:

Molecular weight of 24-mer:

$$24 \times 325 \text{ daltons/nucleotide} = 7,800 \text{ daltons} = 7,800 \text{ g/mol}$$

Number of possible 24-mers:

$$4^{24} = 2.8 \times 10^{14} \text{ molecules}$$

How many molecules of 24-mer in a vial sold by NEB:

$$1 \text{ A}_{260} \text{ unit} = 33 \text{ } \mu\text{g} = 3.3 \times 10^{-5} \text{ g}$$

$$3.3 \times 10^{-5} \text{ g} \div 7,800 \text{ g/mol} = 4.2 \times 10^{-9} \text{ mol}$$

$$(4.2 \times 10^{-9} \text{ mol}) \times (6.02 \times 10^{23} \text{ molecules/mol}) = 2.5 \times 10^{15} \text{ molecules}$$

How many vials needed to sum to 1 of each possible 24-mer:

$$2.8 \times 10^{14} \text{ molecules} \div 2.5 \times 10^{15} \text{ molecules} = 0.11 \text{ vial}$$

Put another way, every vial of Random Primer 24 sold by New England Biolabs would be expected to contain 9 copies of every possible 24-nucleotide sequence. Therefore, Random Primer 24 would contain every possible gene fragment imaginable that is 24 nucleotides in length.

Art Unit: 1635

The Examiner notes the claims are drawn to an "Isolated nucleic acid." However, no clear or limiting definition of the term "isolated" is readily found in the specification that would clearly preclude isolated mixtures of oligonucleotides of the type sold and disclosed by NEB. Given the voluminous nature of the instant application, if Applicant is aware of a definition of the term which would preclude compositions of the type referred to in the instant rejection, Applicant is invited to point to such disclosure in replying to the instant rejection.

Accordingly, the Random Primer 24 sold by New England Biolabs anticipates the instant claims.

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Claims 23, 25, and 27-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Fodor et al. (US Patent 6,582,908, published as US 2001/0053519 A1 on Dec. 20, 2001).

The claims are interpreted as above in the rejection over the NEB Catalog.

Fodor et al. taught nucleic acid arrays comprising all possible 20-mers (see claims 4, 7, and 10; and Example 2, beginning at column 22).

Methods for designing and synthesizing "n-mer" arrays to which are attached all possible nucleic acid sequence of a given length, including such calculations as are necessary to design and synthesize all possible oligonucleotides of a given length are taught at columns 17 and 18, for example. For instance, it is said that a 25-mer array would comprise  $4^{25}$  different oligonucleotide sequences.

At column 22, it is taught that at a feature size of  $10\text{ }\mu\text{m}^2$  square micrometers, all possible 10 mers could fit on a single substrate the size of a dime. At a size of  $1\text{ }\mu\text{m}^2$ , all possible 20 mers would fit on 100  $10\text{ }\mu\text{m}^2$  substrates. "Thus the present technology provides for making a single

Art Unit: 1635

substrate of that size having all one million, seven million or more oligonucleotides, depending on the feature size and the size of the substrate. When the number of desired oligonucleotides is so large that a single substrate is impractical, multiple substrates may be used.”

Each of the oligonucleotides present on the array are considered to be isolated to the extent they are immobilized in their own particular space on the array.

Accordingly, Fodor et al. taught arrays comprising all possible 20-mers. As such, Fodor et al. taught 20-nucleotide DNA equivalents of the instantly claimed nucleic acids. Therefore, Fodor et al. anticipates the instant claims.

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Claim 23 is rejected under 35 U.S.C. 102(e) as being anticipated by Zhou (US Patent 7,250,289).

Zhou discloses a 25-nucleotide DNA, microarray probe, that is at least 70% identical to a complement of SEQ ID NO:348, as claimed in claim 23 (d). See SEQ ID NO: 669995 therein. See also alignment below, also available in SCORE. Zhou discloses that the probe may be RNA or DNA and may be from 8 to 1000 nucleotides in length (column 5).

Therefore, Zhou anticipates the instant claims.

```
RESULT 3
US-10-719-900-669995/c
; Sequence 669995, Application US/10719900
; Patent No. 7250289
; GENERAL INFORMATION:
; APPLICANT: Xue Mei Zhou
; TITLE OF INVENTION: Methods of Genetic Analysis of Mouse
; FILE REFERENCE: 3528.1
; CURRENT APPLICATION NUMBER: US/10/719,900
; CURRENT FILING DATE: 2003-11-20
; PRIOR APPLICATION NUMBER: 60/427,808
; PRIOR FILING DATE: 2002 11 20
; NUMBER OF SEQ ID NOS: 982914
; SOFTWARE: Microarray Probe Sequence Listing Generator V 1.1
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Art Unit: 1635

; Patent No. 7250289  
; SEQ ID NO 669995  
; LENGTH: 25  
; TYPE: DNA  
; ORGANISM: Mus musculus  
US-10-719-900-669995

Query Match 70.9%; Score 15.6; DB 5; Length 25;  
Best Local Similarity 68.2%; Pred. No. 5.1e+02;  
Matches 15; Conservative 3; Mismatches 4; Indels 0; Gaps 0;

Qy 1 CAGCAGCACACUGUGGUUGUA 22  
| | | | | | | | | | | | | : | | : : |  
Db 23 CAGCAGCACACAGTGGACTCTA 2

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Claims 23, 27, 28, 31, 35, and 36 are rejected under 35 U.S.C. 102(e) as being anticipated by Tuschl et al. (US Patent 7,232,806).

Tuschl et al. disclose a 21-nucleotide DNA probe, SEQ ID NO:19, complementary to microRNA mir-15, said to be used for Northern blotting, that is at least 77.3% identical to instant SEQ ID NO:348. See alignment below (also available in SCORE). See columns 4 and 5. The probe therefore defines the corresponding miRNA, as well as its complements. Also disclosed therein are vectors for expressing said miRNAs. See paragraph 39, for example.

Therefore, Tuschl et al. anticipate the instant claims.

Art Unit: 1635

## RESULT 4

US-10-490-955-19

; Sequence 19, Application US/10490955

; Patent No. 7232806

; GENERAL INFORMATION:

; APPLICANT: Tuschl, Thomas

; APPLICANT: Lagos-Quintana, Mariana

; APPLICANT: Lendeckel, Winfried

; APPLICANT: Meyer, Jutta

; APPLICANT: Rauhut, Reinhard

; TITLE OF INVENTION: MicroRNA Molecules

; FILE REFERENCE: 2923-613

; CURRENT APPLICATION NUMBER: US/10/490,955

; CURRENT FILING DATE: 2004-03-29

; PRIOR APPLICATION NUMBER: PCT/EP02/10881

; PRIOR FILING DATE: 2002-09-27

; PRIOR APPLICATION NUMBER: EP 02 016 772.2

; PRIOR FILING DATE: 2002-07-26

; PRIOR APPLICATION NUMBER: EP 02 006 712.0

; PRIOR FILING DATE: 2002-03-22

; PRIOR APPLICATION NUMBER: EP 01 123 453.1

; PRIOR FILING DATE: 2001-09-28

; NUMBER OF SEQ ID NOS: 562

; SOFTWARE: PatentIn version 3.2

; SEQ ID NO 19

; LENGTH: 21

; TYPE: DNA

; ORGANISM: Artificial Sequence

; FEATURE:

; OTHER INFORMATION: Oligonucleotide probe with significant homology to D.

; OTHER INFORMATION: melanogaster, HeLa cell, mouse kidney, adult zebrafish and frog

; OTHER INFORMATION: ovary miR-15

US-10-490-955-19

Query Match 69.1%; Score 15.2; DB 5; Length 21;

Best Local Similarity 60.0%; Pred. No. 7.8e+02;

Matches 12; Conservative 5; Mismatches 3; Indels 0; Gaps 0;

Qy 2 AGCAGCACACUGUGGUUUGU 21

||||||| :||::|:

Db 2 AGCAGCACATAATGGTTTGT 21

**Conclusion**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louis V. Wollenberger whose telephone number is 571-272-8144. The examiner can normally be reached on M-F, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached on (571)272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



Art Unit: 1635

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

LW

Art Unit 1635

September 11, 2007

/Sean M<sup>c</sup>Garry/

Primary Examiner

AU 1635